

Original article

Contribution of Self-Lymphatic Drainage to Subclinical Lymphedema After Treatment for Breast Cancer

Engin Taştaban 💿 *

Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Aydin Adnan Menderes University, Aydin, Turkey

Abstract

Lymphedema is a significant complication of breast cancer treatment. Early treatment of subclinical lymphedema may prevent its related complications. We aimed to evaluate the contribution of applying self-lymphatic drainage (SLD) in subclinical LE patients. One hundred twenty-eight women diagnosed with subclinical lymphedema were enrolled in the study. Patients were allocated into control group 1 (n=64) and SLD group 2 (n=64). Excess volume; the Visual Analog Scale (VAS) for pain, stiffness, heaviness, and tightness; the Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) for disability; handgrip strength; Beck Depression Inventory (BDI) for depression were recorded before and after therapy. Statistically significant improvements in the excess volume were observed in both groups; however, there was a substantial change in the SLD group. Also, only the VAS and BDI scores were assessed significantly lower in the SLD group than in the control group. In conclusion, SLD is useful in reducing lymphedema volume, sensations of pain, stiffness, heaviness, tightness, and depression in patients with subclinical LE. **Keywords:** Subclinical Lymphedema, Self-Lymphatic Drainage, Breast Cancer.

Received: 27 July 2022 * Accepted: 07 September 2022 * DOI: https://doi.org/10.29329/ijiasr.2022.474.1

^{*} Corresponding author:

Tastaban Engin is an associate professor in the Department of Physical Medicine and Rehabilitation at Aydin Adnan Menderes University Faculty of Medicine in Aydin, Turkey. His research interests include the Physical Medicine and Rehabilitation. He has lived, worked, and studied in Aydin, Turkey. Email: engintastaban@gmail.com

INTRODUCTION

Lymphedema (LE) is a chronic, progressive, and debilitating condition caused by impairments in lymph transport (Fish et al., 2020). Cancer treatments such as radiation therapy and resection of lymph nodes can decrease lymph resorption and transport, causing lymphatic insufficiency (Levenhagen et al., 2017). All breast cancer survivors are at risk for LE (Runowicz et al., 2016), and the incidence varies between 9.1-39% (Zhang et al., 2020). Most are diagnosed up to 24 months after the treatment, typically a progressive condition (DiSipio et al., 2013). Stage "0" lymphedema is either a subclinical or latent condition where initial swelling is not evident despite impaired lymphatic transport (Executive Committee of the International Society of Lymphology, 2020). The condition can be transitory and may exist months or years before overt edema occurs.

Management of subclinical LE is likely to prevent the development and complications of clinical LE. In addition, Yamamoto et al. pointed out that subclinical LE could be essential in preventing clinical LE (Yamamoto et al., 2011). Despite the clinical articles supporting the importance of early identification of subclinical LE, there is limited evidence to guide treatment. The current recommendation is that more frequent check-ups and treatment should commence if there is no improvement when the volumeter increases between 5-10% compared to the non-affected arm (Damstra et al., 2017). In subclinical LE, education, and recommendations are given to patients about their risk for apparent LE due to cancer treatment. In addition to the measures mentioned, the main goal of the management of subclinical LE might be to reduce stasis lymph in the interstitium and improve the lymphatic circulation's outflow.

Lymphedema self-management activities, including self-lymphatic drainage (SLD), play an essential role in LE management (Cansiz et al., 2022). Still, its adherence rates are sub-optimal, ranging from 28 to 69% (Zhao et al., 2021). SLD is a simplified version of manual lymphatic drainage (MLD) (Bahtiyarca et al., 2019). SLD is familiar with the pressures and techniques used in MLD. SLD is a hands-on therapy that the patient can easily apply using simplified hand movements in a set sequence. SLD shows its effect as it is in manual lymphatic drainage. SLD helps move fluid from oedematous areas toward the functioning lymphatics (Williams et al., 2002). Unfortunately, the number of studies on the effectiveness of SLD in subclinical LE is limited. In the present study, we aimed to evaluate the contribution of applying SLD in subclinical LE patients.

MATERIALS and METHODS

The study was designed as a randomized controlled trial, as shown in Figure its flow diagram.

Taştaban / Uluslararası Fen Araştırmalarında Yenilikçi Yaklaşımlar Dergisi / International Journal of Innovative Approaches in Science Research, 2022, Vol. 6 (3), 133-144



Figure Flow diagram of the study.

The study protocol was approved by Institutional Ethics Committee with a decision no. 2017/1289. Participants were recruited from University Physical Medicine and Rehabilitation in-patient clinic between December 2017 and April 2022.

Interventions

Inclusion criteria had surgery related to unilateral breast cancer, a new diagnosis of stage 0 LE (less than 2 cm difference at the circumference measurements and/or <10% volume difference between the arms), and completed radiotherapy. Exclusion criteria involved bilateral breast cancer, primer LE, any intervention for LE within 12 months, truncal and/or breast edema, continuing radiotherapy, current infection, metastases, heart failure, arterial and/or venous occlusion. Additional exclusions included insufficient cognitive status, physiotherapy within the last year, cervical-originated upper extremity problems, pregnancy, a pacemaker or any implanted electrical device, renal disease, liver disease, or any medications affecting the body fluid and electrolyte balance. The patients were randomly divided into groups of equal size using "Random Allocation Software" (Version 1.0, May 2004; Department of Anesthesia, Isfahan University of Medical Sciences, Isfahan, Iran).

In the control group, the patients received skincare and exercise. In addition, the patients followed a LE exercise program with breathing exercises, neck and shoulder range of motion, and stretching for levator scapulae, upper trapezius, pectoralis major, and rotator muscles to facilitate lymph circulation. The author supervised the exercises during each therapy session.

In the SLD group, the patients received SLD in combination with skin care and exercises after suture removal and closure of the incision. SLD was performed by subjects for 20 min each day (Williams et al., 2002). The procedure was applied consecutively to the neck, non-affected axilla, anterior chest wall, affected inguinal region, lateral trunk, and lastly, affected shoulder, upper arm, forearm, hand, and fingers. The patients were shown how to use a relaxed hand to gently stretch the skin in the direction away from the swollen area, repeating the movements ten times. The patients performed SLD under the supervision of the author, and their technique was observed daily during the study. A water-based hydrating lotion was used to facilitate the maneuvers and to provide regular skincare. In addition, treatment sessions were instituted at the in-patient clinic during the hospitalization.

The educational supplies consisted of instruction with printed materials about the lymphatic system, the reasons for lymphedema, the identification of possible causing factors, and the to prevent lymphedema (prevention of infection, hand usage, limb elevation, the exercise of the arm, and weight reduction) have given the participants in both groups.

Assessments and outcome measures

Demographic features of the patients, including age, body mass index $[BMI = weight (kg) / height^2 (m^2)]$, duration of lymphedema (month), and the number of axillary lymph nodes removed were all recorded. Subjects followed through screenings for a maximum of three years after surgery.

Assessment of Lymphedema severity as outcome measures of the applied treatment

Circumferential measurements

The truncated cone formula was used to calculate the total volume (V) of the limb, as described earlier (Tastaban et al., 2020)

Volume = $h (C^2 + Cc + c^2) / 12\pi$

Where C is the first circumferential measurement (circumference of the top of the cone), c is the second circumferential measurement (circumference of the base of the cone), and h is the distance from measurement C to c. The same examiner evaluated both arms. An Excel-based software program was used to convert the values into arm volumes in mL.

Percentage excess volume (PEV) is the preferred measure for defining the severity of LE, as described earlier (Tastaban et al., 2020)

 $PEV = [(V_{LE} - V_H) / V_H] \ge 100$

Here, V_{LE} denotes the volume of the LE arm, and V_H is that of the healthy arm. This approach is better than the absolute difference volume and also minimizes the effects of BMI on the volume estimates (Tastaban et al., 2020). The efficacy of the therapeutic intervention was then quantified by the percentage reduction of excess volume (PREV)

 $PREV = [(pre-treatment V_{LE} - post-treatment V_{LE}) / excess volume)] x 100$

Clinical symptoms of pain (activity, resting), stiffness, heaviness, and tightness were evaluated using the Visual Analog Scale (VAS) with a 0–10 Numerical Rating Scale (Sezgin Ozcan et al., 2018). The patients' functional situation was assessed by the Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) outcome questionnaire, which is a self-reported assessment tool for measuring physical function and symptoms in individuals with a musculoskeletal disorder of the upper limb (Martins da Silva & Rezende, 2014). QuickDASH was also reported as a convenient, reliable, and valid patient-reported outcome measure to evaluate upper limb disability in breast cancer patients (LeBlanc et al., 2014). The scores indicate disability and severity, ranging from 0 to 100. Grip strength was measured using a Jamar® hydraulic hand dynamometer (Sammons Preston, Bolingbrook, IL, USA). Both hands of the patient's grip strength were assessed using the second level of resistance (3.75 cm) as the elbow is at 90° flexion and the forearm is neutral (Merchant et al., 2008). All measurements were performed bilaterally and repeated three times. The average of the results was recorded in kg. The clinical depression was evaluated by Beck Depression Inventory (BDI). Scores ranged from 0 to 63, and higher scores indicated depression. The validity and reliability of BDI for the Turkish population have already been tested (Beck et al., 1961).

RESULTS and DISCUSSION

The baseline demographic and clinical characteristics of the patients within the control and SLD groups are shown in Table 1. Intergroup comparison of this pre-treatment data indicated similar characteristics.

Variables	Control group (n=64)	SLD group (n=64)	P value	
Age (years)	55.0 (48.0-58.0)	53.0 (42.0-58.0)	0.206	
Body mass index (kg/m ²)	28.8 (27.8-29.5)	28.6 (27.6-29.5)	0.169	
Duration of lymphedema (months)	12.0 (11.0-14.0)	12.0 (11.0-15.0)	0.296	
Baseline excess volume (mL)	162.5 (137.0-179.0)	163.8 (139.0-181.0)	0.675	
Baseline PEV (%)	5.5 (4.1-7.9)	5.4 (3.8-7.9)	0.633	

Table 1. Baseline demographics of 128 study subjects and clinical characteristics before the treatments.

SLD: Self-lymphatic drainage

The baseline excess volume and PEV values were statistically insignificant between the groups. The post-treatment data were given in Table 2.

Variables	Control group (n=64)	SLD group (n=64)	P value	
Post-treatment excess volume (mL)	154.5 (136.3-178.5)	135.5 (123.5-153.0)	< 0.001	
Post-treatment PEV (%)	5.3 (3.3-7.1)	3.8 (2.8-4.8)	0.002	
PREV (%)	41.3 (39.7-42.2)	43.2 (41.9-49.8)	< 0.001	

Table 2. Intergroup comparisons of volumes after 20 treatment sessions.

PEV: percentage of excess volume, PREV: percent reduction of excess volume

The severity of LE at baseline was similar in both groups (5.5% vs. 5.4%), but after the treatment, excess volume exhibited significant improvement, reducing it from 162.5mL to 154.5 mL in the control group and from 163.8mL to 135.5mL in SLD group. In addition, the PEV decreased from 5.5% to 5.3% in the control group and from 5.4% to 3.5% in the SLD group. After treatment, excess volume and PEV improved significantly in the SLD group. Furthermore, the PREV exhibited significant improvement in the SLD group (43.2%) than the control group (41.3%).

The clinical scores recorded during the study were all listed in Table 3. The results showed significant progress in the overall conditions of the patients in both groups. Still, only the VAS and Beck Depression Inventory scores were assessed significantly lower in the SLD group than in the control group.

Variables	n	Control Group	SLD Group	P value
VAS activity pain				
Baseline	64	3.0 (2.3-5.0)	4.0 (3.0-5.0)	0.149
20 days	64	3.0 (2.0-3.0)	2.0 (1.0-3.0)	0.009
VAS rest pain				
Baseline	64	2.0 (1.3-4.0)	2.0 (1.0-3.0)	0.302
20 days	64	2.0 (2.0-3.0)	2.0 (1.0-3.0)	0.006
VAS stiffness				
Baseline	64	2.0 (1.0-2.0)	2.0 (1.0-2.0)	0.246
20 days	64	2.0 (1.0-2.0)	1.0 (0.0-1.0)	< 0.001
VAS heaviness				
Baseline	64	2.0 (2.0-3.0)	2.0 (1.3-3.0)	0.540
20 days	64	2.0 (1.3-3.0)	2.0 (1.0-3.0)	0.543
•				<0.001
VAS tightness				
Baseline	64	4.0 (3.0-5.3)	5.0 (3.0-6.0)	0.688
20 days	64	2.5 (2.0-3.0)	2.0 (1.0-3.0)	0.048
Grip strength				
Baseline	64	18.5 (18.0-20.0)	19.0 (18.0-20.0)	0.330
20 days	64	21.0 (20.0-23.8)	22.0 (21.0-23.0)	0.241
QuickDASH	<i>C</i> 1	50 0 (40 0 54 0)	52 0 (50 0 52 0)	0.715
Baseline 20 days	64 64	52.0 (49.0-54.0) 26.0 (22.0, 20.0)	52.0 (50.0-53.0)	0.715
20 days	04	30.0 (33.0-39.0)	35.0 (32.3-38.0)	0.069
Beck Depression				
Baseline	64	14.0(12.0-17.0)	15.0(12.3-17.0)	0.460
20 days	64	10.0 (8.0-12.0)	90 (80-110)	0.400
	UT	10.0 (0.0 12.0)	<i></i>	0.017

Table 3.	Changes	in VAS,	grip stren	igth, Qu	ickDASH,	and Becl	k Depres	ssion Inv	ventory s	scores
OuickDASH	: Ouick Disa	abilities of th	e Arm. Shou	lder, and H	Hand, SLD: Se	lf-lymphatic	drainage. V	AS: visual	analog scal	le

In present study, we investigated the effects of SLD in subclinical LE patients. We found that it significantly reduced excess arm volume and decreased VAS and depression scores. The strength of our study is that we prepared detailed and precise SLD prescriptions for each individual.

Lymphedema is a significant complication of breast cancer treatment (Ochalek et al., 2017). Subclinical LE marks the period after the initial insult in which lymphatic fluid transport has begun to deteriorate, but clinical manifestations are not yet apparent (Dixon & Weiler, 2015). Therefore, a good awareness of the importance of subclinical LE may prevent the progression of the disease. Furthermore, early and adequate treatment of subclinical LE allows for improving symptoms, upper extremity functioning, and quality of life because of its transitory property (Bucci et al., 2021).

Lymphedema frequently develops slowly, often with self-reported symptoms, such as heaviness, transient swelling, tightness, and slight volume changes should be screened for early diagnosis (Levenhagen et al., 2017). Once stage I or more clinical lymphedema has become established, it would be progressively worse and more difficult to treat. Can et al. reported that information about LE and its risk factors, skin care, and exercise improves self-reported symptoms, volume measurements, and quality of life in patients with subclinical LE (Gencay Can et al., 2019).

Various reports suggest that post-operative surveillance should be screened closely. Boyages et al. pointed out that understanding the risk of subclinical LE may help with LE screening strategies to prevent progression to clinical LE, which can adversely affect the quality of life (Boyages et al., 2021). Another point of view is that when lymphedema is diagnosed and managed at its earliest stages, the condition can be controlled and the complications minimized (Stout et al., 2011).

Clinical lymphedema progresses over time following cancer treatment. Based on the progressive nature of LE, treatment should be commenced at an early stage, although overtreatment must be avoided (Yamamoto & Koshima, 2013). Borman et al. indicated that the patients suffer from LE for a long time, and most of them have uncontrolled LE at grade 2 and have not received any previous treatment (Borman et al., 2019).

Although clinical LE is incurable, patients with subclinical LE can be managed. However, there is no consensus on the management of subclinical lymphedema. Lymphedema self-management activities such as self-lymphatic drainage are generally seldom performed or practiced at a reduced frequency by patients (Zhao et al., 2021). A previously published study has shown that the rate of manual lymphatic drainage massage is 39% of the women prescribed self-lymphatic drainage massage (Brown et al., 2014). Awareness, skincare, weight management, strength training, and exercise are recommended for secondary prevention of LE (Damstra et al., 2017).

Subclinical LE often may be invisible to patients, and clinical LE progresses over time. Soran et al. concluded that early and sufficient interventions of subclinical LE may prevent the progress to advanced stages and related complications (Soran et al., 2014). The authors also reported that progression to clinical LE occurred in 4.4% in the intervention group, whereas 36.4% in the control group. A recent review concluded that self-lymphatic drainage (SLD), education, exercise, and compression garments are recommended interventions in subclinical LE (Ryans et al., 2021).

A recent study by Temur et al. investigated the effectiveness of lymphedema self-management, including informing, LE evaluation, exercise program, and simple lymphatic drainage in sixty-one patients with upper limb LE (stage 1 and more). After evaluating the patients, they reported significant

improvement in scores of EORTC QLQ-30, QLQ-BRE 23 (European Organization for Research and Treatment of Cancer Core QoL questionnaire), DASH, and LE volumes (Temur & Kapucu, 2019). The authors concluded that the Self-Management of the Lymphedema Program effectively prevents lymphedema development following breast cancer treatment. According to this study, we thought that LE could be managed using effective interventions at any stage, especially in the subclinical stage. Dönmez et al. studied the effect of combined treatment of physical activity program and SLD in patients with breast cancer-related lymphedema (Donmez & Kapucu, 2017). Patients were randomized into 25 patients intervention group (physical activity program and SLD) and 27 patients control group (who did not undergo intervention). After the treatment, there was an evident improvement in symptom severity scores in the intervention group. Therefore, the authors recommended that physical activity programs and SLD can effectively prevent lymphedema. In our study, we did not leave untreated the control group, and we observed significant improvement in both groups. Moreover, the VAS and BDI scores were measured significantly lower in the SLD group. Similarly, the current study results show that VAS scores more significantly improved in the SLD group than in controls. The addition of SLD helps alleviate pain, heaviness, tightness, and depression. The present study's findings indicated that adding SLD was more effective in reducing arm volume and subjective symptoms such as pain, stiffness, heaviness, and tightness, as well as improving depression in patients with subclinical LE.

This study had limitations. First, the study protocol spanned only four weeks; so long-term effects were not monitored. Second, this study was conducted in one rehabilitation clinic. Therefore, multicenter randomized controlled trials with extended follow-up periods should be performed to validate the findings further.

Conclusion

In conclusion, SLD is useful in reducing lymphedema volume, sensations of pain, stiffness, heaviness, tightness, and depression in patients with subclinical LE. However, further research is required to supply more evidence for the efficacy of SLD and to determine the effect of the advice on the patient's quality of life.

REFERENCES

- Bahtiyarca, Z. T., Can, A., Eksioglu, E., & Cakci, A. (2019). The addition of self-lymphatic drainage to compression therapy instead of manual lymphatic drainage in the first phase of complex decongestive therapy for treatment of breast cancer-related lymphedema: A randomized-controlled, prospective study. Turkish journal of physical medicine and rehabilitation, 65(4), 309-317.
- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. Archives of general psychiatry, 4, 561-571.

- Borman P, Moffatt C, Murray S, Yaman A, Denizli M, Dalyan M, Unsal-Delialioğlu S, Eyigör S, Ayhan F, Çakıt BD, Vural S, Özdemir O, Kurt E, Çelik EC, Cerrahoğlu L, Kepekçi M, Terzioğlu F, & Donmez AA. (2019). LIMPRINT Study: The Turkish Experience. Lymphatic research and biology, 17(2), 202-210.
- Boyages, J., Vicini, F. A., Shah, C., Koelmeyer, L. A., Nelms, J. A., & Ridner, S. H. (2021). The Risk of Subclinical Breast Cancer-Related Lymphedema by the Extent of Axillary Surgery and Regional Node Irradiation: A Randomized Controlled Trial. International journal of radiation oncology, biology, physics, 109(4), 987-997.
- Brown, J. C., Cheville, A. L., Tchou, J. C., Harris, S. R., & Schmitz, K. H. (2014). Prescription and adherence to lymphedema self-care modalities among women with breast cancer-related lymphedema. Support Care Cancer, 22(1), 135-143.
- Bucci, L. K., Brunelle, C. L., Bernstein, M. C., Shui, A. M., Gillespie, T. C., Roberts, S. A., Naoum, G. E., & Taghian, A. G. (2021). Subclinical Lymphedema After Treatment for Breast Cancer: Risk of Progression and Considerations for Early Intervention. Annals of surgical oncology, 28(13), 8624-8633.
- Cansiz, G., Arikan Donmez, A., Kapucu, S., & Borman, P. (2022). The effect of a self-management lymphedema education program on lymphedema, lymphedema-related symptoms, patient compliance, daily living activities and patient activation in patients with breast cancer-related lymphedema: A quasi-experimental study. European journal of oncology nursing, 56, 102081.
- Damstra, R. J., Halk, A. B., & Dutch Working Group on, L. (2017). The Dutch lymphedema guidelines based on the International Classification of Functioning, Disability, and Health and the chronic care model. Journal of vascular surgery, 5(5), 756-765.
- DiSipio, T., Rye, S., Newman, B., & Hayes, S. (2013). Incidence of unilateral arm ref after breast cancer: a systematic review and meta-analysis. The Lancet. Oncology, 14(6), 500-515.
- Dixon, J. B., & Weiler, M. J. (2015). Bridging the divide between pathogenesis and detection in lymphedema. Seminars in cell & developmental biology, 38, 75-82.
- Donmez, A. A., & Kapucu, S. (2017). The effectiveness of a clinical and home-based physical activity program and simple lymphatic drainage in the prevention of breast cancer-related lymphedema: A prospective randomized controlled study. European journal of oncology nursing, 31, 12-21.
- Executive Committee of the International Society of Lymphology (2020). The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. Lymphology, 53(1), 3–19.
- Fish, M. L., Grover, R., & Schwarz, G. S. (2020). Quality-of-Life Outcomes in Surgical vs Nonsurgical Treatment of Breast Cancer-Related Lymphedema: A Systematic Review. JAMA surgery, 155(6), 513-519.
- Gencay Can, A., Eksioglu, E., & Cakci, F. A. (2019). Early Detection and Treatment of Subclinical Lymphedema in Patients with Breast Cancer. Lymphatic research and biology, 17(3), 368-373.
- LeBlanc, M., Stineman, M., DeMichele, A., Stricker, C., & Mao, J. J. (2014). Validation of QuickDASH outcome measure in breast cancer survivors for upper extremity disability. Archives of physical medicine and rehabilitation, 95(3), 493-498.

- Levenhagen, K., Davies, C., Perdomo, M., Ryans, K., & Gilchrist, L. (2017). Diagnosis of Upper Quadrant Lymphedema Secondary to Cancer: Clinical Practice Guideline From the Oncology Section of the American Physical Therapy Association. Physical therapy, 97(7), 729-745.
- Martins da Silva, R. C., & Rezende, L. F. (2014). Assessment of impact of late postoperative physical functional disabilities on quality of life in breast cancer survivors. Tumori, 100(1), 87-90.
- Merchant, C. R., Chapman, T., Kilbreath, S. L., Refshauge, K. M., & Krupa, K. (2008). Decreased muscle strength following management of breast cancer. Disability and rehabilitation, 30(15), 1098-1105.
- Ochalek, K., Gradalski, T., & Partsch, H. (2017). Preventing Early Postoperative Arm Swelling and Lymphedema Manifestation by Compression Sleeves After Axillary Lymph Node Interventions in Breast Cancer Patients: A Randomized Controlled Trial. Journal of pain and symptom management, 54(3), 346-354.
- Runowicz, C. D., Leach, C. R., Henry, N. L., Henry, K. S., Mackey, H. T., Cowens-Alvarado, R. L., Cannady,
 R. S., Pratt-Chapman, M. L., Edge, S. B., Jacobs, L. A., Hurria, A., Marks, L. B., LaMonte, S. J.,
 Warner, E., Lyman, G. H., & Ganz, P. A. (2016). American Cancer Society/American Society of
 Clinical Oncology Breast Cancer Survivorship Care Guideline. CA: a cancer journal for clinicians, 66(1), 43-73.
- Ryans, K., Perdomo, M., Davies, C. C., Levenhagen, K., & Gilchrist, L. (2021). Rehabilitation interventions for the management of breast cancer-related lymphedema: developing a patient-centered, evidence-based plan of care throughout survivorship. Journal of cancer survivorship.
- Sezgin Ozcan, D., Dalyan, M., Unsal Delialioglu, S., Duzlu, U., Polat, C. S., & Koseoglu, B. F. (2018). Complex Decongestive Therapy Enhances Upper Limb Functions in Patients with Breast Cancer-Related Lymphedema. Lymphatic research and biology, 16(5), 446-452.
- Soran, A., Ozmen, T., McGuire, K. P., Diego, E. J., McAuliffe, P. F., Bonaventura, M., Ahrendt, G. M., DeGore, L., & Johnson, R. (2014). The importance of detection of subclinical lymphedema for the prevention of breast cancer-related clinical lymphedema after axillary lymph node dissection; a prospective observational study. Lymphatic research and biology, 12(4), 289-294.
- Stout, N. L., Pfalzer, L. A., Levy, E., McGarvey, C., Springer, B., Gerber, L. H., & Soballe, P. (2011). Segmental limb volume change as a predictor of the onset of lymphedema in women with early breast cancer. PM&R, 3(12), 1098-1105.
- Tastaban, E., Soyder, A., Aydin, E., Sendur, O. F., Turan, Y., Ture, M., & Bilgen, M. (2020). Role of intermittent pneumatic compression in the treatment of breast cancer-related lymphoedema: a randomized controlled trial. Clinical rehabilitation, 34(2), 220–228.
- Temur, K., & Kapucu, S. (2019). The effectiveness of lymphedema self-management in the prevention of breast cancer-related lymphedema and quality of life: A randomized controlled trial. European journal of oncology nursing, 40, 22-35.
- Williams, A. F., Vadgama, A., Franks, P. J., & Mortimer, P. S. (2002). A randomized controlled crossover study of manual lymphatic drainage therapy in women with breast cancer-related lymphoedema. European journal of cancer care, 11(4), 254-261.
- Yamamoto, T., & Koshima, I. (2013). Subclinical lymphedema: understanding is the clue to decision making. Plastic and reconstructive surgery, 132(3), 472e-473e.
- Yamamoto, T., Matsuda, N., Doi, K., Oshima, A., Yoshimatsu, H., Todokoro, T., Ogata, F., Mihara, M., Narushima, M., Iida, T., & Koshima, I. (2011). The earliest finding of indocyanine green

lymphography in asymptomatic limbs of lower extremity lymphedema patients secondary to cancer treatment: the modified dermal backflow stage and concept of subclinical lymphedema. Plastic and reconstructive surgery, 128(4), 314e-321e.

- Zhang, X., Oliveri, J. M., & Paskett, E. D. (2020). Features, Predictors, and Treatment of Breast Cancerrelated Lymphedema. Current breast cancer reports, 12(4), 244-254.
- Zhao, H., Wu, Y., Zhou, C., Li, W., Li, X., & Chen, L. (2021). Breast cancer-related lymphedema patient and healthcare professional experiences in lymphedema self-management: a qualitative study. Supportive care in cancer, 29(12), 8027-8044.